UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,098	06/20/2001	Robert Stuart Coffin	117-340	7947

23117 7590 10/13/2006

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Application Number: 09/762,098
Filing Date: June 20, 2001
Appellant(s): COFFIN ET AL.

BioVEX LIMITED
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed June 29, 2004

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings, which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The amendment after final rejection filed on June 20, 2004 has been entered.

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 34-46 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

WO 96/04395A1 Speck et al. Feb. 15, 1996

Moriuchi et al. " Varicella-Zoster Open Reading Frame 10 Protein, the Herpes Simplex Virus VP16 Homolog, Transactivates Herpesvirus Immediated-Early Gene Promoters." Journal of Virology, vol. 67, No. 5 (May 1993), pp. 2739-2746.

Purewal et al. "Equid Herpesvirus 1 and 4 encode Homologs of the Herps Simplex Type 1 virus Transactivator protein, VP16." Virology, vol. 98, (1994), pp. 385-389.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

Claims 34-46 are rejected under 35 U.S.C. 103. This rejection is set forth in a prior Office Action, mailed on 07/29/2003.

1. Claims 34-46 are rejected under 35 U.S.C. 103(a) as being obvious over Speck et al. (WO 96/04395A1), Moriuchi et al. (J. Virol. 1993, Vol. 67, pp. 2739-2746) and Purewal et al. (Virology 1994, Vol. 198, pp. 385-389).

2. The claimed invention is drawn to a method for producing a mutated HSV comprising mutation in its endogenous VP16 gene, and culturing the mutated virus with a complementing cell line that provides the function of the mutated HSV VP16 with a functional equivalent to a non-HSV VP16 polypeptide including gene 12 from equine herpes virus 1 or BTIF from bovine herpes virus. The said HSV also comprises a heterologous sequence and additionally other essential gene mutation including ICP4 and /or ICP27, which is trans-complemented by HSV ICP4 or ICP27 or an equivalent from another herpesvirus. The complementing HSV ICP4 or ICP27 is expressed under a control of MMTV LTR promoter.

3. Speck et al. teach a mutated herpesvirus and a method of making and using the mutant as a recombinant HSV vector, wherein the mutation is to impair the VP16 and one of other essential gene like ICP0, ICP4, ICP27 etc. The vector further comprises a heterologous sequence encoding a therapeutic polypeptide. Speck et al. also teach a pharmaceutical composition comprising the mutated HSV vectors (See lines 6-8 on page 15 and claims 1-15). Speck et al. do not teach to

complement the mutated VP16 with a complementing cell line expressing a functional equivalent of HSV VP16 gene.

4. Moriuchi et al. teach that a HSV VP16 counterpart, VZV open reading frame 10 (ORF10) is able to complement the VP16 mutant HSV in 1814. They disclose two kinds of experiments that demonstrate the function of VZV ORF10 being able to strongly transactivate the HSV IE gene and complement the VP16 mutant HSV in 1814 for propagation in complementing cell line that expresses said counterpart under an inducible promoter (human metallothionein) (See lines 9 on 1st col. through lines 6 on 2nd col. of page 2743-3744). Particularly, Moruichi et al. shows that VZV ORF 10 is able to transactivate the HSV IE gene up to 28 folds higher than the negative control (See page 2742). Moreover, Moriuchi et al. teach that use of HSV VP16 complementing cell line expressing VZV ORF10 is able to enhance the HSV in 1814 particle production up to 10-folds higher compared with a negative control (See page 2744). Moriuchi do not teach to use EHV gene 12 or BHV BTIF for complementing the mutated HSV VP16.

5. Purewal et al. teach other HSV VP16 counterpart, gene 12 of EHV-1 and EHV-4 that is able to strongly transactivate HSV-1 IE gene (See lines 11-32 on 2nd col. of page 387). Purewal et al. explicitly demonstrate that the EHV gene 12 is able to transactivate the HSV IE gene up to 100 to 250 folds higher then a negative control (See pages 387-388).

6. Therefore, it would have been obvious for one with ordinary skill in the art at the time of the invention was filled to be motivated by the cited references for using a complementing cell line that express the HSV VP16 counterpart to propagate the HSV VP16 mutant with a highly expected success. Because Speck et al teach that the VP16 and ICP4 double mutated virus is able to grow well in a complementing cell line expressing ICP4 and/or ICP27. The additional complementing for the defective VP16 with HSV VP16, the counterpart homology of HSV VP16, i.e. VZV ORF10 or EHV-1 gene 12 would provide a better complement for propagating this double mutated HSV-1. In particular, both Moriuchi et al. and Purewal et al. already teach that the counterpart of HSV VP16 from other species is able to complement the mutated VP16 HSB in 1814. Thus, the claimed invention as a whole is still prima facie obvious absence unexpected results.

(11) Response to Argument

7. Appellants traverse the rejection and mainly argue with three aspects summarized set forth below: (1). There was nothing in the cited art to teach or suggest that use of complementing cell line expressing a homologue of VP16 from different species may provide an improved means for propagating mutant HSV vector stocks; (2). The claimed invention is surprising result because one of ordinary skill in the art would not have expected a VP16 homologues from another species is able to transactivate HSV IE gene promoter as effectively as HSV VP16 itself; and (3). None of the cited prior art documents indicates that homologous recombination does not occur between the HSV VP16 gene and the homologue of VP16 from another species.

8. Appellants' argument has been respectfully considered; however, it is not persuasive for the reasons set forth in the following examiner's answer.

9. (1) The cited references teach and suggest the claimed invention. Speck et al. teach a recombinant herpesvirus vector comprising tow mutations in VP16 gene and ICP4 or ICP27 gene. The said vector further comprises heterologous sequence encoding one or more heterologous polypeptides having a therapeutic application (See claims 1-6 and 9-15). Thus, this vector has same structural characteristics to the claimed vector. The references of Moriuchi et al. and Purewal et al. teach to use a VP16 counterpart form other species to transactivate the HSV IE gene and propagate the VP16 mutated HSV in a complementing cell line. In particular, Moriuchi et al. teach that a counterpart of VZV ORF 10 and Purewal et al. teach the counterpart of EHV Gene 12. Moruichi et al. shows that VZV ORF 10 is able to transactivate the HSV IE gene up to 28 folds higher than the negative control (See page 2742); and Purewal et al. demonstrate that the EHV gene 12 is able to transactivate the HSV IE gene up to 100 to 250 folds higher then the negative control (See pages 387-388). Moreover, Moriuchi et al. teach that use of HSV VP16 complementing cell line expressing VZV ORF10 is able to enhance the HSV in 1814 particle production up to 10-folds higher as compared with the negative control (See page 2744).

10. They also teach that HSV-1 gene expression is regulated coordinately and sequentially, progressing from immediate-early (IE) to early, then to late viral genes. The IE genes products are known to play critical roles in HSV-1 gene regulation. Four of five HSV IE genes

transcriptions are induced by a virion structure protein VP16 (See page 2739 of the reference by Moriuchi et al.).

11. It is well known in the art that CAT assay used by Purewal et al. and Moriuchi et al. is a conventional assay, which is particularly designed for testing whether a HSV IE gene can be trans-activated by a transcription factor, such as VP16 counterpart. By successful demonstration that HSV VP16 counterpart is able to strongly transactivate the HSV IE gene, Moruichi et al. further successfully demonstrated and confirmed that the HSV VP16 counterpart, VZV ORF-10-expressing cell lines is able to enhance de nova synthesis of the infectious HSV virus and complement an HSV-1 mutant (in 1814), which lacks the transactivating ability of VP16 (See last paragraph in the right column of page 2739 in the reference by Moriuchi et al.).

12. Therefore, one of ordinary skill in the art would have been motivated to use a complementing cell line that expresses other HSV counterpart VP16 from another species to transactivate HSV IE gene and propagate a VP16 mutated HSV absences unexpected result.

13. (2). The appellants' results are not unexpected. Appellants argue that the claimed method of using VP16 counterpart of EHV g12 to complement the defective HSV VP16 improves the efficiency of VP16 defective HSV in 1814 to the same level as the wild-type HSV (Virus 17+). However, the specification only teaches that the cell line containing EHV-VP 16 complement the growth of VP16 mutated HSV (in 1814) to a certain level (80,000/65,000), which does not reach the level of the wild-type HSV (400,000/250,000), and is less efficient than using the conventional compound HMSA in the growth medium (200,000/90,000). Thus, it is not an unexpected result.

14. Appellants also assert that the improved efficiency by the claimed method for propagating the VP16 mutant HSV observed when EHV gene 12 is present in the complementing cell line was not obvious from the prior art in compared to HMBA. However, this is not an argument because the outstanding 103 rejection is not based on the comparison between the transactivation efficiency by using EHV gene 12 or using HMBA, it is the disclosures of prior art obviously teach and suggest for a person with ordinary skill in the art to use HSV VP16 counterpart from other species and successful transactivate the HSV IE gene and complementing VP16 mutant HSV replication with a complementing cell line absence unexpected result.

Respectfully submitted,

Baoqun Li

Bao Qun Li
October 01, 2006

Conferees
Bruce Campell
Yvonne Eyler

Nixon & Vanderhye
1100 North Glebe Road 8th Floor
Arlington, VA 22201-4714

Bruce Campell

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Yvonne Eyler

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600